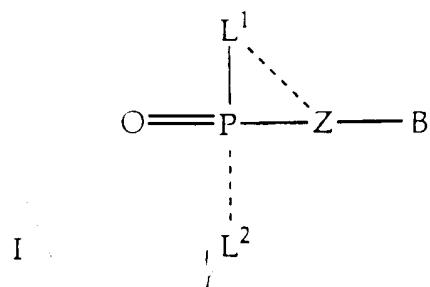


What is claimed is:

1. A compound of the formula I

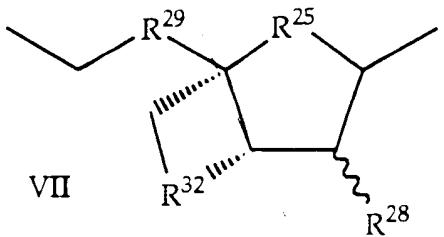
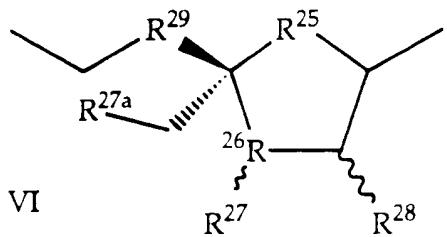
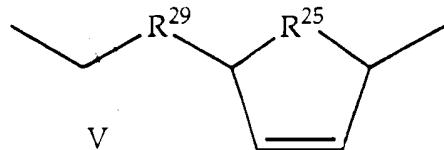
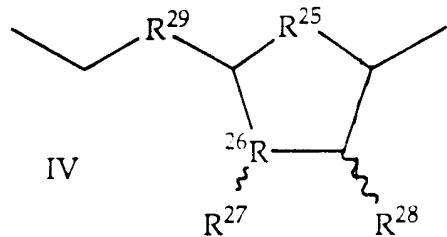


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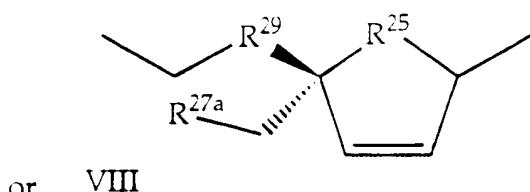
or a physiologically acceptable salt thereof, wherein

L<sup>1</sup> and L<sup>2</sup> are independently an amino acid or polypeptide residue bonded to the phosphorus atom of the compound by an amide bond, or L<sup>1</sup> and L<sup>2</sup> are independently an oxyester, thioester, a substituted or unsubstituted 10 amine, or hydroxy, provided that one or both of L<sup>1</sup> and L<sup>2</sup> is an amino acid or polypeptide residue and provided that any carboxyl group that is linked by less than 5 atoms to the amide N is esterified or amidated and the dotted lines represent facultative bonds;

15 Z is -CHR<sup>7</sup>-R<sup>11</sup>-(CH<sub>2</sub>)<sub>m1</sub>-C<sup>#</sup>(R<sup>8</sup>)((CH<sub>2</sub>)<sub>m2</sub>(R<sup>9</sup>))-(CH<sub>2</sub>)<sub>m3</sub>-R<sup>10</sup>-(CH<sub>2</sub>)<sub>m4</sub>-, -Q-  
C<sub>6</sub>H<sub>4</sub>-CH<sub>2</sub>-, -CHR<sup>7</sup>-O-CHR<sup>7</sup>-O-CHR<sup>7</sup>, -CHR<sup>7</sup>-(CHR<sup>13</sup>)<sub>m1</sub>-CHR<sup>14</sup>-R<sup>10</sup>,



20



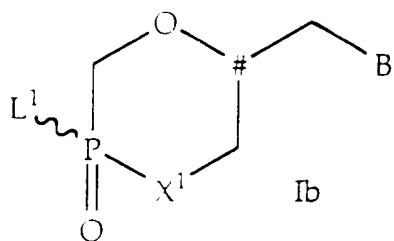
or VIII

5       $R^7$  is H or  $C_1$ - $C_4$  alkyl;  
 $R^8 = R^7$  or  $C_2$ - $C_4$  alkenyl, azidomethyl or azidoethyl;  
 $R^9$  is halogen (F, Cl, Br or I), H or OH;  
 $R^{10}$  is O,  $CH_2$  or a chemical bond;  
 $R^{11}$  is O, S,  $CH_2$ ,  $CHF$ ,  $CF_2$ ;  
 $Q$  is  $-C(R^{12})_2-CH_2-$ ,  $-C(R^{12})_2-O-$ ,  $-CR^{12}=CR^{12}-$ , or  $-C\equiv C-$ , wherein each  $R^{12}$  is independently H, or halogen;  
 $R^{13}$  is H, halogen, OH,  $CH_3$ ,  $CH_2OH$ , or  $C_3$ - $C_{12}$  acyloxymethyl;  
10       $R^{14}$  is independently H, halogen, OH,  $CH_3$ ,  $CH_2OH$ ,  $C_3$ - $C_{12}$  acyloxymethyl, or  $C_2$ - $C_{12}$  acyloxy;  
 $R^{25}$  is  $CH_2$ ,  $CHF$  or O;  
 $R^{26}$  is CH or S, provided that when  $R^{25}$  is CH,  $R^{26}$  is not S;  
 $R^{27}$  is H, OH, halogen,  $N_3$ ,  $C_1$ - $C_4$  alkyl,  $C_1$ - $C_4$  alkoxy or when,  $R^{26}$  is S,  
15       $R^{27}$  is absent;  
 $R^{27a}$  is H, OH, halogen,  $N_3$ ,  $C_1$ - $C_4$  alkyl,  $C_1$ - $C_4$  alkoxy;  
 $R^{28} = R^{27a}$  and is independently chosen;  
 $R^{29}$  is O, S,  $CH_2$ ,  $CHF$ ,  $CF_2$ ;  
 $R^{32}$  is O;  
20       $m_1 = m_2 = m_3 = m_4$  is an integer having a value from 0 to 4 wherein each is independently chosen;  
        the carbon atom designated  $C^{\#}$  has linked substituents that are in the R, S or RS configuration; and  
        B is a heterocyclic base.

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2.      A compound of the formula Ib



and stereoisomers and salts of such compounds wherein

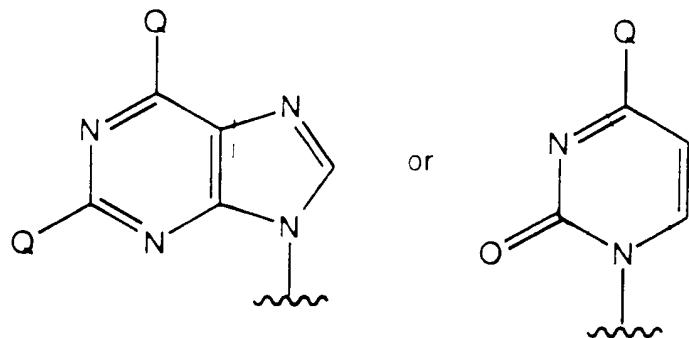
$X^1$  is O or S;

5       $L^1$  is an amino acid, a polypeptide residue, a substituted or unsubstituted amine, an oxyester or a thio ester; and

the carbon atom designated # has linked substituents that are in the R, S or RS configuration, provided that  $L^1$  is not a C<sub>1</sub>-C<sub>4</sub> alkyl ester or, when when B is cytosin-1-yl, then  $L^1$  is not OCH<sub>2</sub>C(O)NR<sup>5a</sup><sub>2</sub>, OCH<sub>2</sub>C(O)OR<sup>5a</sup>, OCH<sub>2</sub>OC(O)R<sup>5a</sup>, OCH(R<sup>5a</sup>)OC(O)R<sup>5a</sup> (R, S or RS stereochemistry),

10     OCH<sub>2</sub>C(R<sup>5a</sup>)<sub>2</sub>CH<sub>2</sub>OH, OCH<sub>2</sub>OR<sup>5a</sup>, OR<sup>5a</sup>, NHR<sup>5a</sup> or NR<sup>5a</sup><sub>2</sub> wherein R<sup>5a</sup> is C<sub>1</sub>-C<sub>20</sub> alkyl, aryl or aryl-alkyl which may be substituted or unsubstituted by substituents independently selected from the group consisting of hydroxy and halogen, and provided that when  $X^1$  is O and B is adenine, cytosine, guanine, thymine, uracil, 2,6-diamino purine, hypoxanthine, or Z<sup>2</sup>; wherein Z<sup>2</sup> is

15

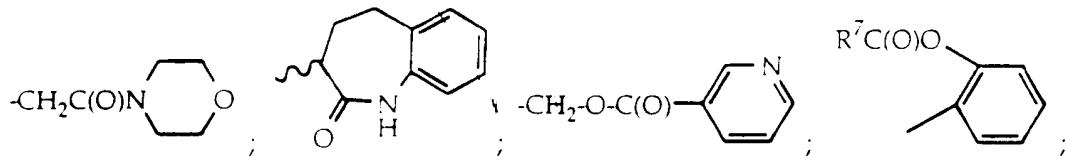


Q is independently chosen from H, Cl, NHR<sup>X</sup>, NR<sup>X</sup><sub>2</sub>, NHC(O)R<sup>X</sup>, N(C(O)R<sup>X</sup>)<sub>2</sub>, OH or NCHN(R<sup>X</sup>)<sub>2</sub>, then  $L^1$  is not OR<sup>Y</sup>, NH<sub>2</sub>, NHR<sup>X</sup>, or N(R<sup>X</sup>)<sub>2</sub>

20     where R<sup>Y</sup> represents a physiologically hydrolyzable ester group selected from the group consisting of CH<sub>2</sub>C(O)N(R<sup>X</sup>)<sub>2</sub>, CH<sub>2</sub>C(O)OR<sup>X</sup>, CH<sub>2</sub>OC(O)R<sup>X</sup>, CH(R<sup>X</sup>)OC(O)R<sup>X</sup>, CH<sub>2</sub>C(R<sup>X</sup>)<sub>2</sub>CH<sub>2</sub>OH, or CH<sub>2</sub>OR<sup>X</sup>; R<sup>Y</sup> may also be R<sup>X</sup> provided that R<sup>Y</sup> and R<sup>X</sup> are not simultaneously alkyl;

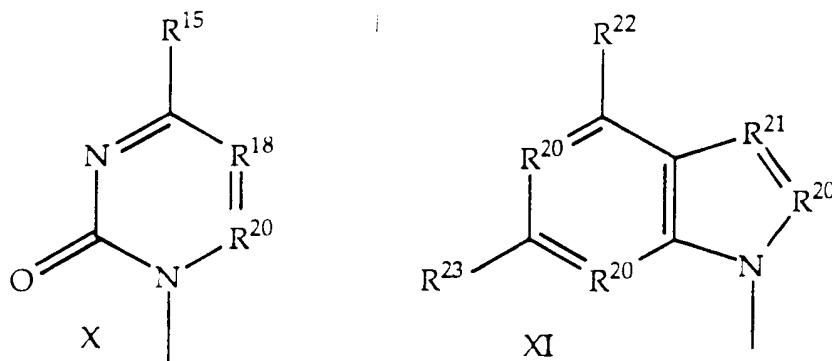
$R^X$  represents  $C_1-C_{20}$  alkyl, aryl or aryl-alkyl which may be substituted or unsubstituted by substituents independently selected from the group consisting of hydroxy, oxygen, nitrogen and halogen.

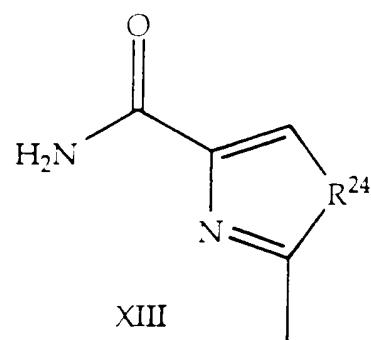
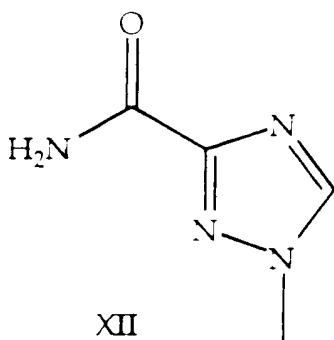
5        3.     The compound of claim 2 wherein  $L^1$  is  $NHR^{40}$  or  $OR^{31}$  wherein  
 $R^{40}$  is  $C_{1-20}$  alkyl;  
 $R^{31}$  is 2,3-dihydro-6-hydroxyindene; sesamol; catechol monoester;  
 $-CH_2-C(O)-N(R^7)_2$  wherein each  $R^7$  the same or different;  $-CH_2-S(O)(R^7)$ ;  $-CH_2-S(O)_2(R^7)$ ;  $-O-CH_2-CH(OC(O)CH_2R^7)-CH_2(OC(O)CH_2R^7)$ ; cholesteryl; a  
10      monosaccharide; a disaccharide; an oligosaccharide (3 to 9 monosaccharide residues), enolpyruvate; glycerol; an  $\alpha$ -D- $\beta$ -diglyceride; trimethoxybenzyl; triethoxybenzyl; 2-alkyl pyridinyl ( $C_{1-4}$  alkyl);



15       $C_3-C_6$  aryl substituted by 3, 4 or 5 halogen atoms or 1 or 2 atoms or groups selected from halogen,  $C_1-C_{12}$  alkoxy, cyano, nitro, OH,  $C_1-C_{12}$  haloalkyl,  $C_1-C_{12}$  alkyl,  $C_2-C_{12}$  alkenyl or  $C_2-C_{12}$  alkynyl; or  
20       $C_1-C_4$  alkylene- $C_3-C_6$  aryl substituted in the aryl moiety by 3 to 5 halogen atoms or 1 to 2 atoms or groups selected from halogen,  $C_1-C_{12}$  alkoxy, cyano, nitro, OH,  $C_1-C_{12}$  haloalkyl,  $C_1-C_{12}$  alkyl,  $C_2-C_{12}$  alkenyl or  $C_2-C_{12}$  alkynyl.

4.     The compound of claim 3 wherein B is





wherein R<sup>15</sup> is H, OH, F, Cl, Br, I, OR<sup>16</sup>, SH, SR<sup>16</sup>, NH<sub>2</sub>, or NHR<sup>17</sup>;

R<sup>16</sup> is C<sub>1</sub> - C<sub>6</sub> alkyl

5 R<sup>17</sup> is C<sub>1</sub> - C<sub>6</sub> alkyl;

R<sup>18</sup> is N, CF, CCl, CBr, Cl, CR<sup>19</sup> or CSR<sup>19</sup>, COR<sup>19</sup>;

10 R<sup>19</sup> is H, C<sub>1</sub> - C<sub>9</sub> alkyl, C<sub>2</sub> - C<sub>9</sub> alkenyl, C<sub>2</sub> - C<sub>9</sub> alkynyl or C<sub>7</sub> - C<sub>9</sub> aryl-alkyl unsubstituted or substituted by OH, O, N, F, Cl, Br or I;

R<sup>20</sup> is N or CH;

15 R<sup>21</sup> is N, CH, CCN, CCF<sub>3</sub>, CC≡CH or CC(O)NH<sub>2</sub>;

R<sup>22</sup> is H, OH, NH<sub>2</sub>, SH, SCH<sub>3</sub>, SCH<sub>2</sub>CH<sub>3</sub>, SCH<sub>2</sub>CCH, SCH<sub>2</sub>CHCH<sub>2</sub>, SC<sub>3</sub>H<sub>7</sub>, NH(CH<sub>3</sub>), N(CH<sub>3</sub>)<sub>2</sub>, NH(CH<sub>2</sub>CH<sub>3</sub>), N(CH<sub>2</sub>CH<sub>3</sub>)<sub>2</sub>, NH(CH<sub>2</sub>CCH), NH(CH<sub>2</sub>CHCH<sub>2</sub>), NH(C<sub>3</sub>H<sub>7</sub>) or halogen;

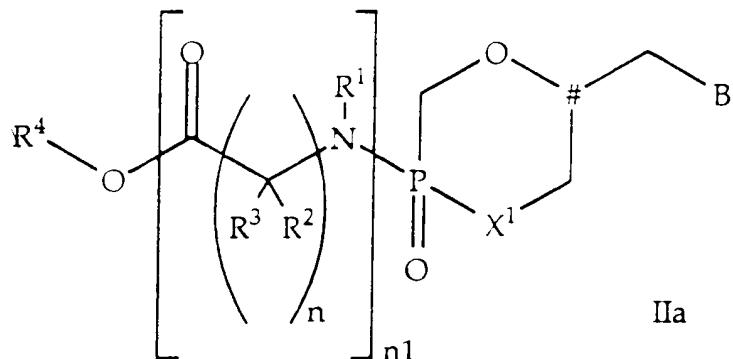
R<sup>23</sup> is H, OH, F, Cl, Br, I, SCH<sub>3</sub>, SCH<sub>2</sub>CH<sub>3</sub>, SCH<sub>2</sub>CCH, SCH<sub>2</sub>CHCH<sub>2</sub>, SC<sub>3</sub>H<sub>7</sub>, OR<sup>16</sup>, NH<sub>2</sub>, or NHR<sup>17</sup>; and

20 R<sup>24</sup> is O, S or Se.

5. The compound of claim 4 wherein B is cytosin-1-yl, 6-azacytosin-1-yl, 5-fluorocytosin-1-yl, adenin-9-yl, guanin-9-yl or 2, 6-diaminopurin-9-yl.

6. The compound of claim 4 wherein R<sup>31</sup> is 2-methoxyphenyl, 3-methoxyphenyl, 4-methoxyphenyl, 2-fluorophenyl, 3-fluorophenyl, 4-fluorophenyl, 2-ethoxy-5-hydroxyphenyl, 2-ethoxy-4-hydroxyphenyl, 3,5-dimethoxyphenyl, 2,4-difluorophenyl, 2-(haloalkyl)-phenyl, 3-(haloalkyl)phenyl, 4-(haloalkyl)-phenyl, 2-cyanophenyl, 3-cyanophenyl, 4-cyanophenyl, 2-ethoxyphenyl, 3-ethoxyphenyl, 4-ethoxyphenyl, 2-carboethoxyphenyl, 3-carboethoxyphenyl, 4-carboethoxyphenyl, or 2-haloalkylbenzyl, 3-haloalkylbenzyl or 4-haloalkylbenzyl.

7. The compound of claim 2 of the formula IIa



5 wherein

n is 1, 2, 3, 4 or 5, wherein for n > 1, each -C(R<sup>2</sup>)(R<sup>3</sup>) is the same or different;

n1 is an integer;

10 R<sup>1</sup> is H or C<sub>1</sub>-C<sub>9</sub> alkyl which is unsubstituted or substituted by substituents independently selected from the group consisting of OH, O, N, COOR<sup>4</sup> and halogen, C<sub>3</sub>-C<sub>6</sub> aryl which is unsubstituted or substituted by substituents independently selected from the group consisting of OH, O, N, COOR<sup>4</sup> and halogen or C<sub>3</sub>-C<sub>9</sub> aryl-alkyl which is unsubstituted or substituted by substituents independently selected from the group consisting of OH, O, N, COOR<sup>4</sup> and halogen;

15 R<sup>2</sup> = R<sup>1</sup> and is independently chosen;

20 R<sup>3</sup> is C(O)-OR<sup>4</sup>, amino, C<sub>1</sub> - C<sub>3</sub> alkylamino, C<sub>1</sub> - C<sub>3</sub> alkyldiamino, C<sub>1</sub> - C<sub>6</sub> alkenylamino, hydroxy, thiol, C<sub>1</sub> - C<sub>3</sub> alkoxy, C<sub>1</sub> - C<sub>3</sub> alkthiol, (CH<sub>2</sub>)<sub>n</sub>COOR<sup>4</sup>, C<sub>1</sub>-C<sub>6</sub> alkyl which is unsubstituted or substituted with OH, halogen, SH, NH<sub>2</sub>, phenyl, hydroxyphenyl or C<sub>7</sub> - C<sub>10</sub> alkoxyphenyl; C<sub>2</sub>-C<sub>6</sub> alkenyl which is unsubstituted or substituted with OH, halogen, SH, NH<sub>2</sub>, phenyl, hydroxyphenyl or C<sub>7</sub> - C<sub>10</sub> alkoxyphenyl; C<sub>6</sub>-C<sub>12</sub> aryl which is unsubstituted or substituted with OH, halogen, SH, NH<sub>2</sub>, phenyl, hydroxyphenyl or C<sub>7</sub> - C<sub>10</sub> alkoxyphenyl; and

25 R<sup>4</sup> is H provided that n1 greater than 1, or is C<sub>3</sub>-C<sub>9</sub> alkyl which is substituted by substituents independently selected from the group consisting of OH, O, N and halogen, C<sub>3</sub>-C<sub>6</sub> aryl which is substituted by substituents independently selected from the group consisting of OH, O, N and halogen or

$C_3$ - $C_9$  aryl-alkyl which is substituted by substituents independently selected from the group consisting of OH, O, N and halogen.

8. The compound of claim 7 wherein

5 n and n1 are 1;

R<sup>1</sup> is H, methyl, phenyl or benzyl;

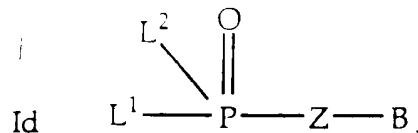
R<sup>2</sup> is H;

R<sup>3</sup> is H, -CH<sub>3</sub>, -CH(CH<sub>3</sub>)<sub>2</sub>, -CH<sub>2</sub>-CH(CH<sub>3</sub>)<sub>2</sub>, -CHCH<sub>3</sub>-CH<sub>2</sub>-CH<sub>3</sub>, -CH<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>, -CH<sub>2</sub>CH<sub>2</sub>-S-CH<sub>3</sub>, -CH<sub>2</sub>OH, -CH(OH)-CH<sub>3</sub>, -CH<sub>2</sub>-SH, -CH<sub>2</sub>-C<sub>6</sub>H<sub>4</sub>OH, -CH<sub>2</sub>-CO-NH<sub>2</sub>, -CH<sub>2</sub>-CH<sub>2</sub>-CO-NH<sub>2</sub>, -CH<sub>2</sub>-COOH, -CH<sub>2</sub>-CH<sub>2</sub>-COOH, -(CH<sub>2</sub>)<sub>4</sub>-NH<sub>2</sub>, -<sub>10</sub>(CH<sub>2</sub>)<sub>3</sub>-NH-C(NH<sub>2</sub>)-NH<sub>2</sub>, 1-guanidinoprop-3-yl, benzyl, 4-hydroxybenzyl, imidazol-4-yl, indol-3-yl, methoxyphenyl or ethoxyphenyl; and

R<sup>4</sup> is methyl, ethyl, propyl, isopropyl, butyl, t-butyl, phenyl, benzyl, 1-pyridyl, 3-pyridyl, 1-pyrimidinyl, pivaloyloxymethyl, N-ethylmorpholino, N-2-propylmorpholino, methoxyethyl, 4-N-methylpiperidyl, 3-N-methylpiperidyl, 2-, 3-, or 4-N,N-dimethylaminophenyl, 2-, 3-, or 4-N,N-diethylaminophenyl or 1-ethylpiperazinyl.

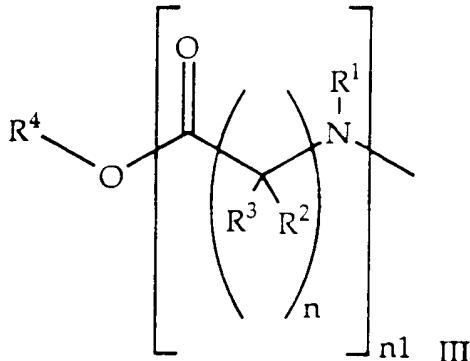
9. The compound of claim 8 wherein B is cytosin-1-yl, 6-azacytosin-1-yl, adenin-9-yl, guanin-9-yl or 2, 6-diaminopurin-9-yl, and X<sup>1</sup> is O.

20 10. The compound of claim 1 of the formula Id



25

11. The compound of claim 10 wherein L<sup>1</sup> is of the formula III



wherein

n is 1, 2, 3, 4 or 5, wherein for n > 1, each -C(R<sup>2</sup>)(R<sup>3</sup>) is the same or different;

n1 is an integer;

5 R<sup>1</sup> is H or C<sub>1</sub>-C<sub>9</sub> alkyl which is unsubstituted or substituted by substituents independently selected from the group consisting of OH, O, N, COOR<sup>4</sup> and halogen, C<sub>3</sub>-C<sub>6</sub> aryl which is unsubstituted or substituted by substituents independently selected from the group consisting of OH, O, N, COOR<sup>4</sup> and halogen or C<sub>3</sub>-C<sub>9</sub> aryl-alkyl which is unsubstituted or substituted 10 by substituents independently selected from the group consisting of OH, O, N, COOR<sup>4</sup> and halogen;

R<sup>2</sup> = R<sup>1</sup> and is independently chosen;

R<sup>3</sup> is C(O)-OR<sup>4</sup>, amino, C<sub>1</sub> - C<sub>3</sub> alkylamino, C<sub>1</sub> - C<sub>3</sub> alkyldiamino, C<sub>1</sub> - C<sub>6</sub> alkenylamino, hydroxy, thiol, C<sub>1</sub> - C<sub>3</sub> alkoxy, C<sub>1</sub> - C<sub>3</sub> alkthiol, (CH<sub>2</sub>)<sub>n</sub>COOR<sup>4</sup>,

15 C<sub>1</sub>-C<sub>6</sub> alkyl which is unsubstituted or substituted with OH, halogen, SH, NH<sub>2</sub>, phenyl, hydroxyphenyl or C<sub>7</sub> - C<sub>10</sub> alkoxyphenyl; C<sub>2</sub>-C<sub>6</sub> alkenyl which is unsubstituted or substituted with OH, halogen, SH, NH<sub>2</sub>, phenyl, hydroxyphenyl or C<sub>7</sub> - C<sub>10</sub> alkoxyphenyl; C<sub>6</sub>-C<sub>12</sub> aryl which is unsubstituted or substituted with OH, halogen, SH, NH<sub>2</sub>, phenyl, hydroxyphenyl or C<sub>7</sub> - C<sub>10</sub> 20 alkoxyphenyl; and

R<sup>4</sup> is H provided that n1 greater than 1, or is C<sub>3</sub>-C<sub>9</sub> alkyl which is substituted by substituents independently selected from the group consisting of OH, O, N and halogen, C<sub>3</sub>-C<sub>6</sub> aryl which is substituted by substituents independently selected from the group consisting of OH, O, N and halogen or 25 C<sub>3</sub>-C<sub>9</sub> aryl-alkyl which is substituted by substituents independently selected from the group consisting of OH, O, N and halogen;

L<sup>2</sup> is OR, SR or is the same as L<sup>1</sup> wherein,

R is H,

C<sub>3</sub>-C<sub>24</sub> acyloxyalkyl,

30 C<sub>6</sub>-C<sub>24</sub> acyloxyarylalkyl,

C<sub>3</sub>-C<sub>24</sub> acyloxyalkoxyalkyl,

C<sub>3</sub>-C<sub>24</sub> acyloxyhaloalkyl,

C<sub>1</sub>-C<sub>20</sub> alkyl which is unsubstituted or substituted by substituents independently selected from the group consisting of OH, O, N and halogen (F, 35 Cl, Br, I),

$C_3$ - $C_{20}$  aryl which is unsubstituted or substituted by substituents independently selected from the group consisting of  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  alkoxy,  $C_1$ - $C_6$  haloalkyl (1 to 3 halogen atoms), cyano, nitro,  $OH$ ,  $O$ ,  $N$  and halogen, or

5  $C_4$ - $C_{20}$  aryl-alkyl which is unsubstituted or substituted in the aryl moiety by substituents independently selected from the group consisting of  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  alkoxy,  $C_1$ - $C_6$  haloalkyl (1 to 3 halogen atoms), cyano, nitro,  $OH$ ,  $O$ ,  $N$  and halogen.

12. The compound of claim 11 wherein

10  $n$  and  $n_1$  are 1;

$R$  is  $N$ -ethylmorpholino, pivaloyloxymethyl, phenyl, benzyl, isopropyl, t-butyl, ethyl, isopropyl, butyl, adamantoyloxymethyl, 3-methoxyphenyl, 2-carboethoxyphenyl, 4-fluorophenyl, 2,4-difluorophenyl, 3,5-dimethoxyphenyl, 2,4-dichlorophenyl, 2-ethoxyphenyl, 3-dimethylaminophenyl, 4-trifluoromethylbenzyl, 2-ethylsalicyl,  $-O-CH_2-O-C(O)-C_{10}H_{15}$ ,  $-C_6H_4-CH_2-$   $N(CH_3)_2$ ,  $-CH_2-CH_2F$ ,  $-CH_2-CH_2Cl$ ,  $-CH_2-CF_3$ ,  $R^5$ ,  $NHR^6$  or  $N(R^6)_2$  wherein,

$R^5$  is  $CH_2C(O)N(R^6)_2$ ,  $CH_2C(O)OR^6$ ,  $CH_2OC(O)R^6$ ,  $CH(R^6)OC(O)R^6$ ,  $CH_2C(R^6)_2CH_2OH$ , or  $CH_2OR^6$ , and

20  $R^6$  is  $C_1$ - $C_{20}$  alkyl which is unsubstituted or substituted by substituents independently selected from the group consisting of  $OH$ ,  $O$ ,  $N$  and halogen (1 to 5 halogen atoms),  $C_6$ - $C_{20}$  aryl which is unsubstituted or substituted by substituents independently selected from the group consisting of  $OH$ ,  $O$ ,  $N$  and halogen (1 to 5 halogen atoms) or  $C_7$ - $C_{20}$  aryl-alkyl which is unsubstituted or substituted by substituents independently selected from the group consisting of  $OH$ ,  $O$ ,  $N$  and halogen (1 to 5 halogen atoms);

25  $R^1$  is  $H$ , methyl, ethyl, isopropyl, phenyl or benzyl;

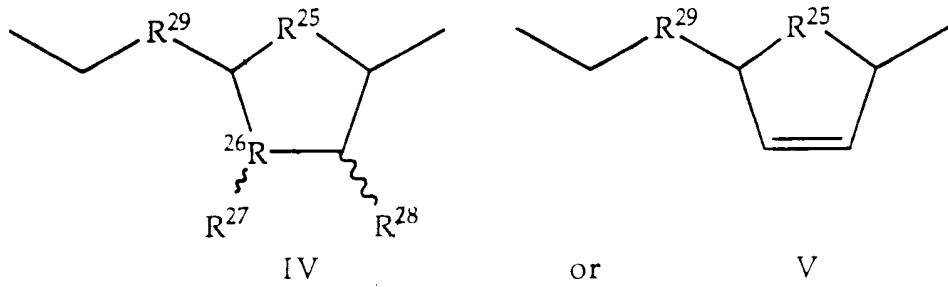
$R^2$  is  $H$ ;

30  $R^3$  is  $H$ ,  $-CH_3$ ,  $-CH(CH_3)_2$ ,  $-CH_2-CH(CH_3)_2$ ,  $-CHCH_3-CH_2-CH_3$ ,  $-CH_2-C_6H_5$ ,  $-CH_2CH_2-S-CH_3$ ,  $-CH_2OH$ ,  $-CH(OH)-CH_3$ ,  $-CH_2-SH$ ,  $-CH_2-C_6H_4OH$ ,  $-CH_2-CO-NH_2$ ,  $-CH_2-CH_2-CO-NH_2$ ,  $-CH_2-COOH$ ,  $-CH_2-CH_2-COOH$ ,  $-(CH_2)_4-NH_2$ ,  $-(CH_2)_3-NH-C(NH_2)-NH_2$ , 1-guanidinoprop-3-yl, benzyl, 4-hydroxybenzyl, imidazol-4-yl, indol-3-yl, methoxyphenyl or ethoxyphenyl; and

35  $R^4$  is methyl, ethyl, propyl, isopropyl, butyl, t-butyl, phenyl, benzyl, 1-pyridyl, 3-pyridyl, 1-pyrimidinyl, pivaloyloxymethyl,  $N$ -ethylmorpholino,  $N$ -

2-propylmorpholino, methoxyethyl, 4-N-methylpiperidyl, 3-N-methylpiperidyl, 2-, 3-, and 4-N,N-dimethylaminophenyl and 2-, 3-, and 4-N,N-diethylaminophenyl or 1-ethylpiperazinyl.

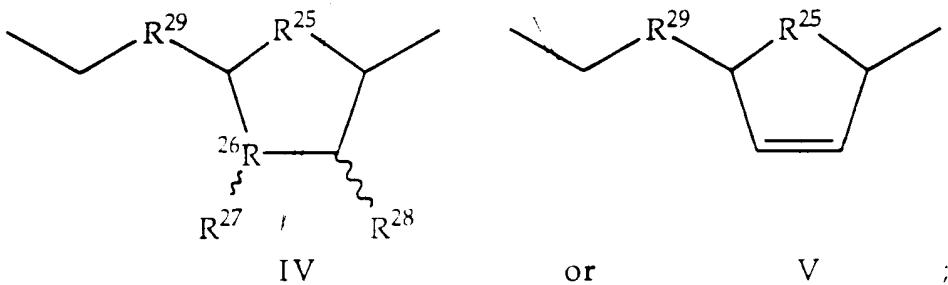
5 13. The compound of claim 12 wherein Z is  $-\text{CHR}^7-\text{R}^{11}-(\text{CH}_2)_{m1}-$   
 $\text{C}(\text{R}^8)((\text{CH}_2)_{m2}(\text{R}^9))-(\text{CH}_2)_{m3}-\text{R}^{10}-(\text{CH}_2)_{m4}-$ ,



10

14. The compound of claim 13 wherein  
Z is  $-\text{CH}_2-\text{O}-\text{CH}_2-\text{CH}_2-$ ,  $-\text{CH}_2-\text{O}-\text{CH}_2-\text{CH}(\text{CH}_2\text{OH})-$ ,  $-\text{CH}_2-\text{O}-\text{CH}_2-$   
 $\text{CH}(\text{CH}_2\text{F})-$ ,  $-\text{CH}_2-\text{O}-\text{CH}_2-\text{CH}(\text{CH}_3)-$ ,  $-\text{CH}_2-\text{O}-\text{CH}_2-\text{CH}(\text{CH}=\text{CH}_2)-$  or  $-\text{CH}_2-\text{O}-$   
 $\text{CH}_2-\text{CH}(\text{CH}_2\text{N}_3)-$ , or is of formula IV or V

15



wherein

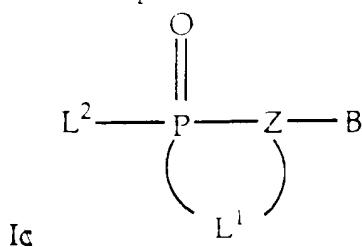
20 R<sup>25</sup> and R<sup>29</sup> are O;

R<sup>26</sup> is CH;

R<sup>27</sup> and R<sup>28</sup> are H; and

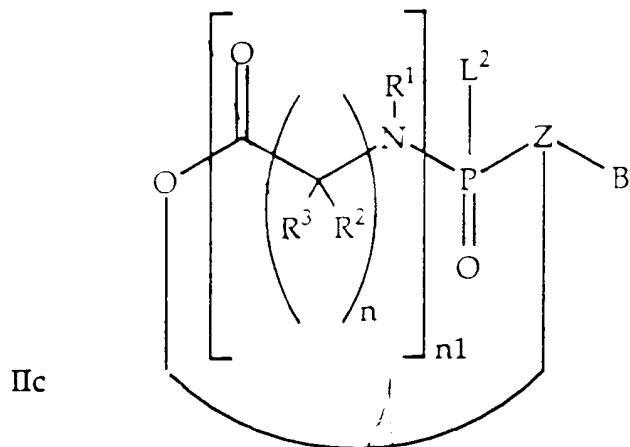
25 B is adenin-9-yl, 1-deazaadenin-9-yl, 3-deazaadenin-9-yl, 7-deaza-8-azaadenin-9-yl, 8-azaadenin-9-yl, guanin-9-yl, 2, 6-diaminopurin-9-yl, 2-aminopurin-9-yl, thymin-1-yl, cytosin-1-yl, 5-fluorocytosin-1-yl, 6-azacytosin-1-yl, 5-methylcytosin-1-yl, 5-bromovinyluracil-1-yl, 5-fluorouracil-1-yl or 5-trifluoromethyluracil-1-yl.

15. The compound of claim 1 of the formula Ic



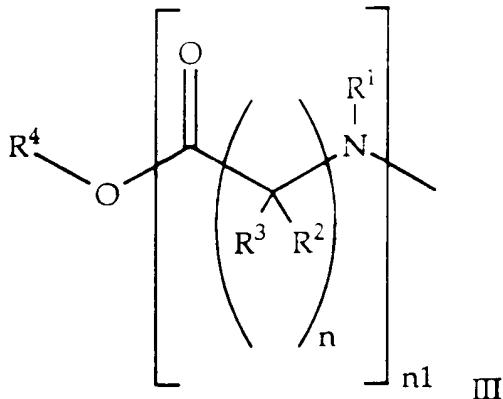
16. The compound of claim 15 of the formula IIc

5



wherein L<sup>2</sup> is OR, SR or

10



wherein

R is H,

C<sub>3</sub>-C<sub>24</sub> acyloxyalkyl,

C<sub>6</sub>-C<sub>24</sub> acyloxyarylalkyl,

C<sub>3</sub>-C<sub>24</sub> acyloxyalkoxyalkyl,

15

C<sub>3</sub>-C<sub>24</sub> acyloxyhaloalkyl,

C<sub>1</sub>-C<sub>20</sub> alkyl which is unsubstituted or substituted by substituents independently selected from the group consisting of OH, O, N and halogen (F, Cl, Br, I),

5 C<sub>3</sub>-C<sub>20</sub> aryl which is unsubstituted or substituted by substituents independently selected from the group consisting of C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> haloalkyl (1 to 3 halogen atoms), cyano, nitro, OH, O, N and halogen, or

10 C<sub>4</sub>-C<sub>20</sub> aryl-alkyl which is unsubstituted or substituted in the aryl moiety by substituents independently selected from the group consisting of C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> haloalkyl (1 to 3 halogen atoms), cyano, nitro, OH, O, N and halogen; and

15 R<sup>1</sup> is O-C<sub>6</sub>H<sub>4</sub>-CH<sub>2</sub>-N(CH<sub>3</sub>)<sub>2</sub>, OR<sup>5</sup>, NHR<sup>6</sup> or N(R<sup>6</sup>)<sub>2</sub> wherein R<sup>5</sup> is CH<sub>2</sub>C(O)N(R<sup>6</sup>)<sub>2</sub>, CH<sub>2</sub>C(O)OR<sup>6</sup>, CH<sub>2</sub>OC(O)R<sup>6</sup>, CH(R<sup>6</sup>)OC(O)R<sup>6</sup>, CH<sub>2</sub>C(R<sup>6</sup>)<sub>2</sub>CH<sub>2</sub>OH, or CH<sub>2</sub>OR<sup>6</sup>, and wherein R<sup>6</sup> is C<sub>1</sub>-C<sub>20</sub> alkyl, C<sub>6</sub>-C<sub>20</sub> aryl or C<sub>7</sub>-C<sub>20</sub> aryl-alkyl which is unsubstituted or substituted by substituents independently selected from the group consisting of OH, O, N and halogen.

17. A compound of the formula (OR<sup>31</sup>)<sub>2</sub>P(O)-Z<sup>1</sup>-B or (OR)(OR<sup>31</sup>)P(O)-Z<sup>1</sup>-B, wherein;

20 B is a heterocyclic base;

Z<sup>1</sup> is selected from the group consisting of -CH<sub>2</sub>-O-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-O-C#H(CH<sub>2</sub>OH)-CH<sub>2</sub>-, -CH<sub>2</sub>-O-C#H(CH<sub>3</sub>)-CH<sub>2</sub>-, -CH<sub>2</sub>-O-C#H(CH<sub>2</sub>F)-CH<sub>2</sub>-, -CH<sub>2</sub>-O-C#H(CH=CH<sub>2</sub>)-CH<sub>2</sub>- and -CH<sub>2</sub>-O-C#H(CH<sub>2</sub>N<sub>3</sub>)-CH<sub>2</sub>;

R is H,

25 C<sub>3</sub>-C<sub>24</sub> 1-acyloxy-1-alkyl,

C<sub>6</sub>-C<sub>24</sub> 1-acyloxy-1-aryl-1-alkyl,

C<sub>3</sub>-C<sub>24</sub> 1-acyloxy-2-alkoxy-1-alkyl,

C<sub>3</sub>-C<sub>24</sub> 1-acyloxy-2-halo-1-alkyl,

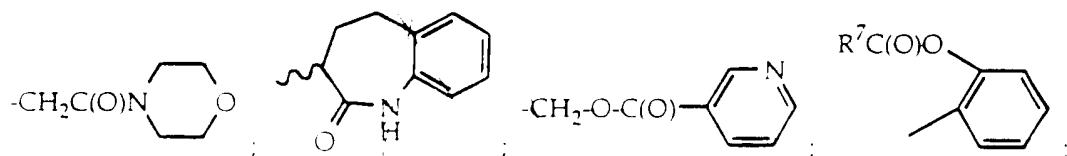
30 C<sub>1</sub>-C<sub>20</sub> alkyl which is unsubstituted or substituted by substituents independently selected from the group consisting of OH, O, N and halogen (F, Cl, Br, I),

C<sub>3</sub>-C<sub>20</sub> aryl which is unsubstituted or substituted by substituents independently selected from the group consisting of C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> haloalkyl, cyano, nitro, OH, O, N and halogen, or

$C_4$ - $C_{20}$  aryl-alkyl which is unsubstituted or substituted in the aryl moiety by substituents independently selected from the group consisting of  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  alkoxy,  $C_1$ - $C_6$  haloalkyl, cyano, nitro, OH, O, N and halogen;

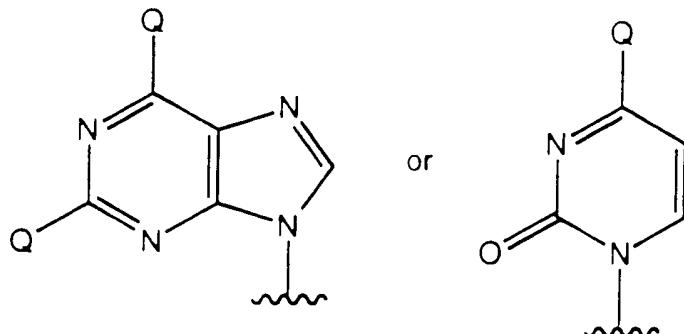
$R^{31}$  is 2,3-dihydro-6-hydroxyindene; sesamol; catechol monoester;

5  $-CH_2-C(O)-N(R^7)_2$  wherein each  $R^7$  is hydrogen or  $C_1$ - $C_4$  alkyl and is the same or different;  $-CH_2-S(O)(R^7)$ ;  $-CH_2-S(O)_2(R^7)$ ;  $-O-CH_2-CH(OC(O)CH_2R^7)-CH_2(OC(O)CH_2R^7)$ ; cholesteryl; a monosaccharide; a disaccharide; an oligosaccharide (3 to 9 monosaccharide residues), enolpyruvate; glycerol; an  $\alpha$ -D- $\beta$ -diglyceride; trimethoxybenzyl; triethoxybenzyl; 2-alkyl pyridinyl ( $C_1$ - $C_4$  alkyl);



$C_3$ - $C_6$  aryl substituted by 3, 4 or 5 halogen atoms or 1 or 2 atoms or groups selected from halogen,  $C_1$ - $C_{12}$  alkoxy, cyano, nitro, OH,  $C_1$ - $C_{12}$  haloalkyl,  $C_1$ - $C_{12}$  alkyl,  $C_2$ - $C_{12}$  alkenyl or  $C_2$ - $C_{12}$  alkynyl; or

15  $C_1$ - $C_4$  alkylene- $C_3$ - $C_6$  aryl substituted in the aryl moiety by 3 to 5 halogen atoms or 1 to 2 atoms or groups selected from halogen,  $C_1$ - $C_{12}$  alkoxy, cyano, nitro, OH,  $C_1$ - $C_{12}$  haloalkyl,  $C_1$ - $C_{12}$  alkyl,  $C_2$ - $C_{12}$  alkenyl or  $C_2$ - $C_{12}$  alkynyl, provided that when  $Z^1$  is  $-CH_2-O-CH_2-CH_2-$  and B is adenin-9-yl, both  $R^{31}$  are not 4-nitrobenzyl or 4-trifluoromethyl-benzyl, and provided that when  $Z^1$  is  $-CH_2-O-CH_2-CH_2-$ ,  $-CH_2-O-C#H(CH_2OH)-CH_2-$ ,  $-CH_2-O-C#H(CH_3)-CH_2-$ ,  $-CH_2-O-C#H(CH_2F)-CH_2-$  or  $-CH_2-O-C#H(CH=CH_2)-CH_2-$  and B is adenine, cytosine, guanine, thymine, uracil, 2,6-diamino purine, hypoxanthine, or  $Z^2$ ; wherein  $Z^2$  is



Q is independently chosen from H, Cl, NHR<sup>X</sup>, NR<sup>X</sup><sub>2</sub>, NHC(O)R<sup>X</sup>, N(C(O)R<sup>X</sup>)<sub>2</sub>, OH or NCHN(R<sup>X</sup>)<sub>2</sub>, then L<sup>1</sup> is not ORY, NH<sub>2</sub>, NHR<sup>X</sup>, or N(R<sup>X</sup>)<sub>2</sub> where R<sup>Y</sup> represents a physiologically hydrolyzable ester group selected from the group consisting of CH<sub>2</sub>C(O)N(R<sup>X</sup>)<sub>2</sub>, CH<sub>2</sub>C(O)OR<sup>X</sup>, CH<sub>2</sub>OC(O)R<sup>X</sup>, CH(R<sup>X</sup>)OC(O)R<sup>X</sup>, CH<sub>2</sub>C(R<sup>X</sup>)<sub>2</sub>CH<sub>2</sub>OH, or CH<sub>2</sub>OR<sup>X</sup>; R<sup>Y</sup> may also be R<sup>X</sup> provided that R<sup>Y</sup> and R<sup>X</sup> are not simultaneously alkyl;

5 R<sup>X</sup> represents C<sub>1</sub>-C<sub>20</sub> alkyl, aryl or aryl-alkyl which may be substituted or unsubstituted by substituents independently selected from the group consisting of hydroxy, oxygen, nitrogen and halogen.

10

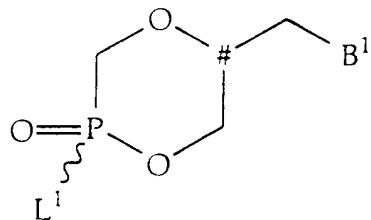
18. The compound of claim 17 wherein R<sup>31</sup> is 2-methoxyphenyl, 3-methoxyphenyl, 4-methoxyphenyl, 2-fluorophenyl, 3-fluorophenyl, 4-fluorophenyl, 2-ethoxy-5-hydroxyphenyl, 2-ethoxy-4-hydroxyphenyl 3,5-dimethoxyphenyl, 2,4-difluorophenyl, 2-(haloalkyl)-phenyl, 3-(haloalkyl)phenyl, 4-(haloalkyl)-phenyl, 2-cyanophenyl, 3-cyanophenyl, 4-cyanophenyl, 2-ethoxyphenyl, 2-carboethoxyphenyl, 3-carboethoxyphenyl, 4-carboethoxyphenyl, or 2-haloalkylbenzyl, 3-haloalkylbenzyl or 4-haloalkylbenzyl.

20

19. The compound of claim 18 wherein B is cytosin-1-yl, 6-azacytosin-1-yl, 5-fluorocytosin-1-yl, adenin-9-yl, guanin-9-yl or 2, 6-diaminopurin-9-yl.

25

20. A compound of the formula (L<sup>1</sup>)<sub>2</sub>P(O)-Z-B<sup>1</sup> or

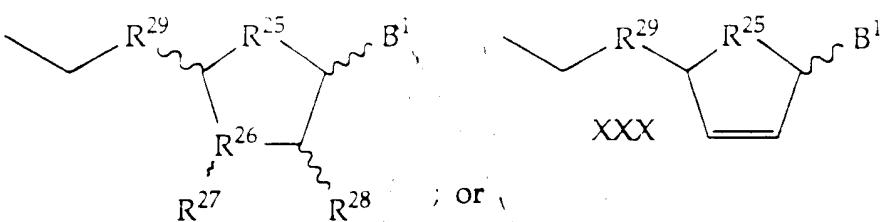
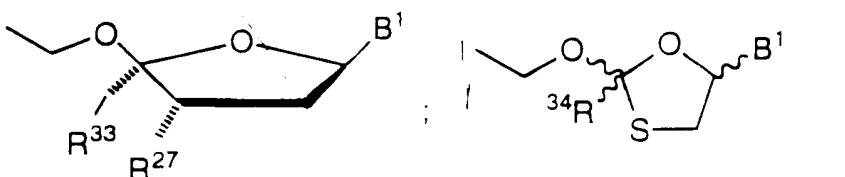
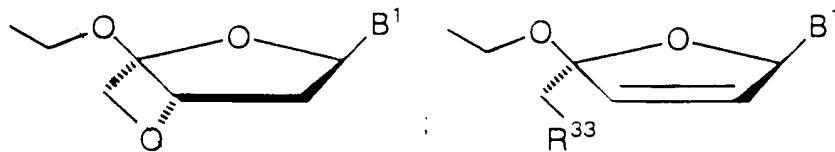


wherein

substituents linked to the carbon atom designated # are in the R, S or 30 RS configuration;

L<sup>1</sup> is independently an amino acid, a polypeptide, an oxyester, a thioester or a substituted or unsubstituted amine;

$B^1$  is a protected heterocyclic base; and  
 $Z-B^1$  is



5

wherein

$R^{27}$  is H, OH, halogen,  $N_3$ ,  $C_1-C_4$  alkyl,  $C_1-C_4$  alkoxy or when,  $R^{26}$  is S,  $R^{27}$  is absent;

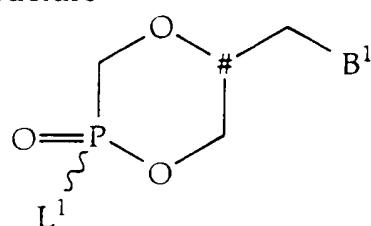
10

$R^{28}$  is H, OH, halogen,  $N_3$ ,  $C_1-C_4$  alkyl or  $C_1-C_4$  alkoxy;

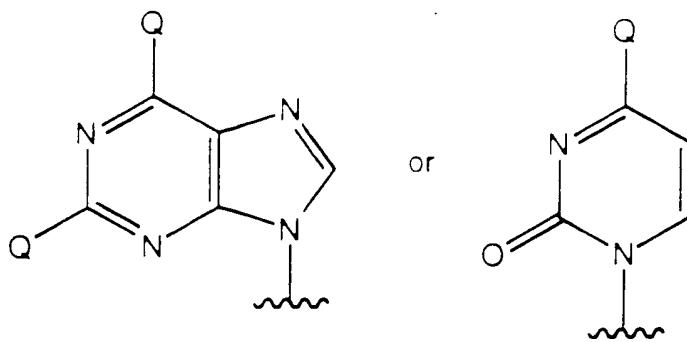
$R^{29}$  is O, S,  $CH_2$ ,  $CHF$  or  $CF_2$ ;

$R^{33}$  is H, OH,  $TBSO$ , halogen, cyano,  $CH_2N_3$ ,  $C_1-C_4$  alkyl,  $C_1-C_4$  alkoxy,  $CH_2OH$  or azido; and

15  $R^{34}$  is H,  $CH_2CN$  or  $CF_3$ , with the proviso that, for structure XXX, when  $R^{25}$  is O or  $CH_2$  and  $R^{29}$   $CH_2$  or O,  $L^1$  is not H or  $C_1-C_6$  alkyl, provided that for compounds of structure



when  $B^1$  is



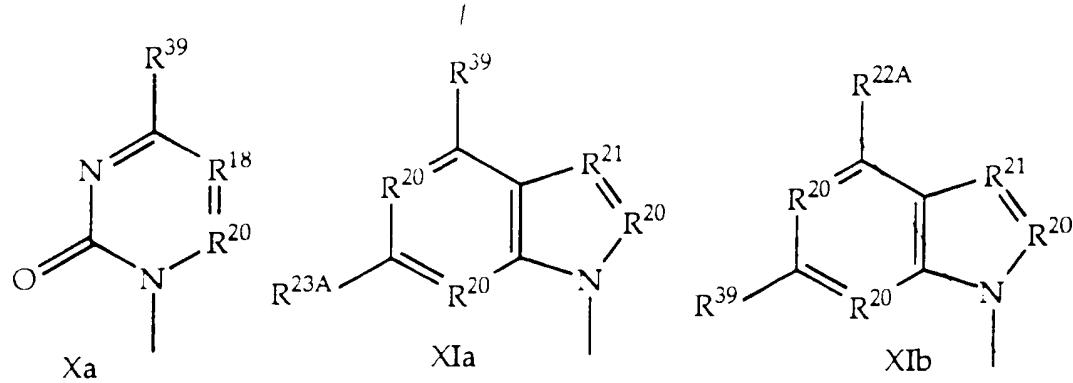
wherein Q is independently chosen from H, Cl, NHR<sup>X</sup>, NR<sup>X</sup><sub>2</sub>, NHC(O)R<sup>X</sup>, N(C(O)R<sup>X</sup>)<sub>2</sub>, OH or NCHN(R<sup>X</sup>)<sub>2</sub>, then L<sup>1</sup> is not OR<sup>Y</sup>, NH<sub>2</sub>, NHR<sup>X</sup>, 5 or N(R<sup>X</sup>)<sub>2</sub> where R<sup>Y</sup> represents a physiologically hydrolyzable ester group selected from the group consisting of CH<sub>2</sub>C(O)N(R<sup>X</sup>)<sub>2</sub>, CH<sub>2</sub>C(O)OR<sup>X</sup>, CH<sub>2</sub>OC(O)R<sup>X</sup>, CH(R<sup>X</sup>)OC(O)R<sup>X</sup>, CH<sub>2</sub>C(R<sup>X</sup>)<sub>2</sub>CH<sub>2</sub>OH, or CH<sub>2</sub>OR<sup>X</sup>; R<sup>Y</sup> may also be R<sup>X</sup> provided that R<sup>Y</sup> and R<sup>X</sup> are not simultaneously alkyl;

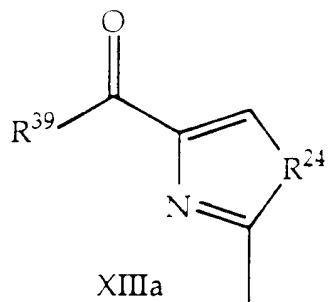
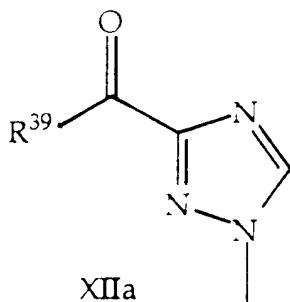
10 R<sup>X</sup> represents C<sub>1</sub>-C<sub>20</sub> alkyl, aryl or aryl-alkyl which may be substituted or unsubstituted by substituents independently selected from the group consisting of hydroxy, oxygen, nitrogen and halogen;

provided that when R<sup>25</sup> is O, R<sup>29</sup> is CH<sub>2</sub>, R<sup>26</sup> is CH, R<sup>27</sup> is OH, R<sup>28</sup> is H or F, and B is adenine, thymine, guanine, cytosine or protected adenine, 15 protected guanine or protected cytosine, both L<sup>1</sup> are not H, methyl or phenyl.

15

21. The compound of claim 20 wherein B<sup>1</sup> is





wherein

R<sup>18</sup> is N, CF, CCl, CBr, Cl, CR<sup>19</sup> or CSR<sup>19</sup>, COR<sup>19</sup>;

5 R<sup>20</sup> is N or CH;

R<sup>21</sup> is N, CH, CCN, CCF<sub>3</sub>, CC≡CH or CC(O)NH<sub>2</sub>;

R<sup>22A</sup> is R<sup>39</sup> or R<sup>22</sup> provided that R<sup>22</sup> is not NH<sub>2</sub>;

10 R<sup>22</sup> is H, OH, NH<sub>2</sub>, SH, SCH<sub>3</sub>, SCH<sub>2</sub>CH<sub>3</sub>, SCH<sub>2</sub>CCH, SCH<sub>2</sub>CHCH<sub>2</sub>, SC<sub>3</sub>H<sub>7</sub>, NH(CH<sub>3</sub>), N(CH<sub>3</sub>)<sub>2</sub>, NH(CH<sub>2</sub>CH<sub>3</sub>), N(CH<sub>2</sub>CH<sub>3</sub>)<sub>2</sub>, NH(CH<sub>2</sub>CCH),

15 NH(CH<sub>2</sub>CHCH<sub>2</sub>), NH(C<sub>3</sub>H<sub>7</sub>) or halogen (F, Cl, Br or I);  
R<sup>23A</sup> is R<sup>39</sup> or R<sup>23</sup> provided that R<sup>23</sup> is not NH<sub>2</sub>;

R<sup>23</sup> is H, OH, F, Cl, Br, I, SCH<sub>3</sub>, SCH<sub>2</sub>CH<sub>3</sub>, SCH<sub>2</sub>CCH, SCH<sub>2</sub>CHCH<sub>2</sub>, SC<sub>3</sub>H<sub>7</sub>, OR<sup>16</sup>, NH<sub>2</sub>, or NHR<sup>17</sup>;

R<sup>24</sup> is O, S or Se; and

15 R<sup>39</sup> is NHR<sup>40</sup>, NHC(O)R<sup>36</sup> or NCR<sup>41</sup>N(R<sup>38</sup>)<sub>2</sub> wherein,

R<sup>36</sup> is C<sub>1</sub>-C<sub>19</sub> alkyl, C<sub>1</sub>-C<sub>19</sub> alkenyl, C<sub>3</sub>-C<sub>10</sub> aryl, adamantoyl, alkylaryl, or C<sub>3</sub>-C<sub>10</sub> aryl substituted with 1 or 2 atoms or groups selected from halogen, methyl, ethyl, methoxy, ethoxy, hydroxy and cyano;

20 R<sup>38</sup> is C<sub>1</sub>-C<sub>10</sub> alkyl, or both R<sup>38</sup> together are 1-morpholino, 1-piperidine or 1-pyrrolidine;

R<sup>40</sup> is C<sub>1</sub>-20 alkyl; and

R<sup>41</sup> is hydrogen or CH<sub>3</sub>.

22. The compound of claim 21 wherein L<sup>1</sup> is R or R<sup>31</sup> wherein

25 R is

C<sub>3</sub>-C<sub>24</sub> 1-acyloxy-1-alkyl,

C<sub>6</sub>-C<sub>24</sub> 1-acyloxy-1-aryl-1-alkyl,

C<sub>3</sub>-C<sub>24</sub> 1-acyloxy-2-alkoxy-1-alkyl,

C<sub>3</sub>-C<sub>24</sub> 1-acyloxy-2-halo-1-alkyl,

$C_1$ - $C_{20}$  alkyl which is unsubstituted or substituted by substituents independently selected from the group consisting of OH, O, N and halogen (F, Cl, Br, I),

5  $C_3$ - $C_{20}$  aryl which is unsubstituted or substituted by substituents independently selected from the group consisting of  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  alkoxy,  $C_1$ - $C_6$  haloalkyl (1 to 3 halogen atoms), cyano, nitro, OH, O, N and halogen,

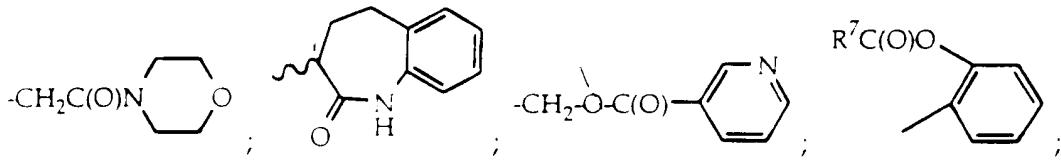
10  $C_4$ - $C_{20}$  aryl-alkyl which is unsubstituted or substituted in the aryl moiety by substituents independently selected from the group consisting of  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  alkoxy,  $C_1$ - $C_6$  haloalkyl (1 to 3 halogen atoms), cyano, nitro, OH, O, N and halogen,

$C_3$ - $C_6$  aryl substituted by 3 to 5 halogen atoms or 1 to 2 atoms or groups independently selected from the group consisting of halogen,  $C_1$ - $C_{12}$  alkoxy, cyano, nitro, hydroxy,  $C_1$ - $C_{12}$  haloalkyl,  $C_1$ - $C_{12}$  alkyl,  $C_2$ - $C_{12}$  alkenyl or  $C_2$ - $C_{12}$  alkynyl, or

15  $C_1$ - $C_4$  alkylene- $C_3$ - $C_6$  aryl substituted in the aryl moiety by 3 to 5 halogen atoms or 1 to 2 atoms or groups independently selected from the group consisting of halogen,  $C_1$ - $C_{12}$  alkoxy, cyano, nitro, hydroxy,  $C_1$ - $C_{12}$  haloalkyl,  $C_1$ - $C_{12}$  alkyl,  $C_2$ - $C_{12}$  alkenyl or  $C_2$ - $C_{12}$  alkynyl; and

20  $R^{31}$  is 2,3-dihydro-6-hydroxyindene; sesamol; catechol monoester;  $-CH_2-C(O)-N(R^7)_2$  wherein each  $R^7$  the same or different;  $-CH_2-S(O)(R^7)$ ;  $-CH_2-S(O)_2(R^7)$ ;  $-O-CH_2-CH(O-C(O)CH_2R^7)-CH_2(OC(O)CH_2R^7)$ ; cholesteryl; a monosaccharide; a disaccharide; an oligosaccharide (3 to 9 monosaccharide residues), enolpyruvate; glycerol; an  $\alpha$ -D- $\beta$ -diglyceride; trimethoxybenzyl; triethoxybenzyl; 2-alkyl pyridinyl ( $C_1$ - $4$  alkyl);

25

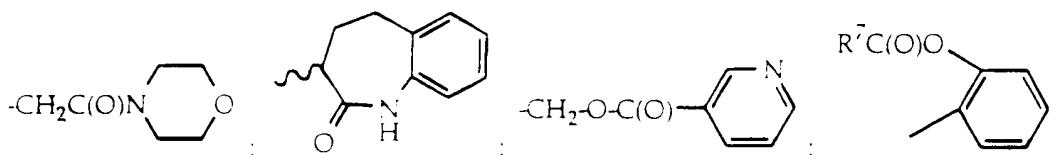


$C_3$ - $C_6$  aryl substituted by 3, 4 or 5 halogen atoms or 1 or 2 atoms or groups selected from halogen,  $C_1$ - $C_{12}$  alkoxy, cyano, nitro, OH,  $C_1$ - $C_{12}$  haloalkyl,  $C_1$ - $C_{12}$  alkyl,  $C_2$ - $C_{12}$  alkenyl or  $C_2$ - $C_{12}$  alkynyl; or

30  $C_1$ - $C_4$  alkylene- $C_3$ - $C_6$  aryl substituted in the aryl moiety by 3 to 5 halogen atoms or 1 to 2 atoms or groups selected from halogen,  $C_1$ - $C_{12}$  alkoxy, cyano, nitro, OH,  $C_1$ - $C_{12}$  haloalkyl,  $C_1$ - $C_{12}$  alkyl,  $C_2$ - $C_{12}$  alkenyl or  $C_2$ - $C_{12}$  alkynyl.

23. The compound of claim 21 wherein L<sup>1</sup> is ethylglycine or N-methylglycine.

24. A compound of the formula (OR<sup>35</sup>)(OR<sup>35</sup>)P(O)-Z-B, wherein;  
5 B is a heterocyclic base;  
R<sup>35</sup> is independently R or R<sup>31</sup>, wherein R is independently  
H,  
C<sub>3</sub>-C<sub>24</sub> 1-acyloxy-1-alkyl,  
C<sub>6</sub>-C<sub>24</sub> 1-acyloxy-1-aryl-1-alkyl,  
10 C<sub>3</sub>-C<sub>24</sub> 1-acyloxy-2-alkoxy-1-alkyl,  
C<sub>3</sub>-C<sub>24</sub> 1-acyloxy-2-halo-1-alkyl,  
C<sub>1</sub>-C<sub>20</sub> alkyl which is unsubstituted or substituted by substituents  
independently selected from the group consisting of OH, O, N and halogen (F,  
Cl, Br, I),  
15 C<sub>3</sub>-C<sub>20</sub> aryl which is unsubstituted or substituted by substituents  
independently selected from the group consisting of C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy,  
C<sub>1</sub>-C<sub>6</sub> haloalkyl (1 to 3 halogen atoms), cyano, nitro, OH, O, N and halogen,  
C<sub>4</sub>-C<sub>20</sub> aryl-alkyl which is unsubstituted or substituted in the aryl  
moiety by substituents independently selected from the group consisting of  
20 C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> haloalkyl (1 to 3 halogen atoms), cyano, nitro,  
OH, O, N and halogen, ,  
25 C<sub>3</sub>-C<sub>6</sub> aryl substituted by 3 to 5 halogen atoms or 1 to 2 atoms or  
groups independently selected from the group consisting of halogen, C<sub>1</sub>-C<sub>12</sub>  
alkoxy, cyano, nitro, hydroxy, C<sub>1</sub>-C<sub>12</sub> haloalkyl, C<sub>1</sub>-C<sub>12</sub> alkyl, C<sub>2</sub>-C<sub>12</sub> alkenyl or  
C<sub>2</sub>-C<sub>12</sub> alkynyl, or  
C<sub>1</sub>-C<sub>4</sub> alkylene-C<sub>3</sub>-C<sub>6</sub> aryl substituted in the aryl moiety by 3 to 5  
halogen atoms or 1 to 2 atoms or groups independently selected from the  
group consisting of halogen, C<sub>1</sub>-C<sub>12</sub> alkoxy, cyano, nitro, hydroxy, C<sub>1</sub>-C<sub>12</sub>  
haloalkyl, C<sub>1</sub>-C<sub>12</sub> alkyl, C<sub>2</sub>-C<sub>12</sub> alkenyl or C<sub>2</sub>-C<sub>12</sub> alkynyl;  
30 R<sup>31</sup> is 2,3-dihydro-6-hydroxyindene; sesamol; catechol monoester;  
-CH<sub>2</sub>-C(O)-N(R<sup>7</sup>)<sub>2</sub> wherein each R<sup>7</sup> the same or different; -CH<sub>2</sub>-S(O)(R<sup>7</sup>); -CH<sub>2</sub>-  
S(O)<sub>2</sub>(R<sup>7</sup>); -O-CH<sub>2</sub>-CH(OC(O)CH<sub>2</sub>R<sup>7</sup>)-CH<sub>2</sub>(OC(O)CH<sub>2</sub>R<sup>7</sup>); cholesteryl; a  
monosaccharide; a disaccharide; an oligosaccharide (3 to 9 monosaccharide  
residues), enolpyruvate; glycerol; an  $\alpha$ -D- $\beta$ -diglyceride; trimethoxybenzyl;  
35 triethoxybenzyl; 2-alkyl pyridinyl (C<sub>1</sub>-C<sub>4</sub> alkyl);

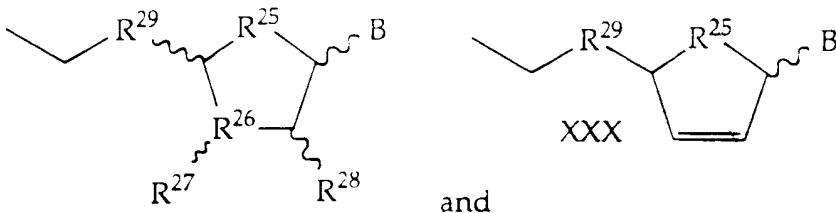
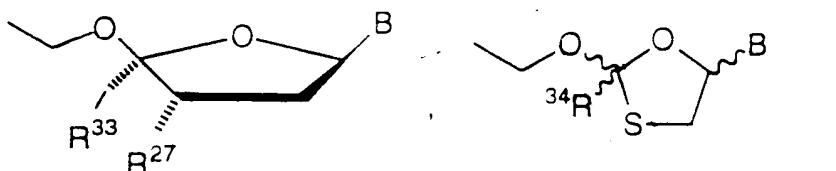
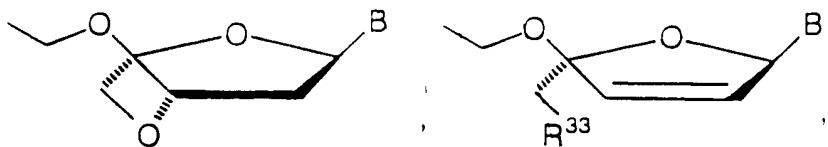


14  $C_3$ - $C_6$  aryl substituted by 3, 4 or 5 halogen atoms or 1 or 2 atoms or groups selected from halogen,  $C_1$ - $C_{12}$  alkoxy, cyano, nitro, OH,  $C_1$ - $C_{12}$  haloalkyl,  $C_1$ - $C_{12}$  alkyl,  $C_2$ - $C_{12}$  alkenyl or  $C_2$ - $C_{12}$  alkynyl; or

5  $C_1$ - $C_4$  alkylene- $C_3$ - $C_6$  aryl substituted in the aryl moiety by 3 to 5 halogen atoms or 1 to 2 atoms or groups selected from halogen,  $C_1$ - $C_{12}$  alkoxy, cyano, nitro, OH,  $C_1$ - $C_{12}$  haloalkyl,  $C_1$ - $C_{12}$  alkyl,  $C_2$ - $C_{12}$  alkenyl or  $C_2$ - $C_{12}$  alkynyl;

$Z$ - $B$  is selected from the group consisting of

10



and

15

wherein

substituents linked to the carbon atom designated # are in the  $R$ ,  $S$  or  $RS$  configuration,

$R^{25}$  is  $CH_2$ ,  $CHF$  or  $O$ ;

$R^{26}$  is  $CH$  or  $S$ , provided that when  $R^{25}$  is  $CH$ ,  $R^{26}$  is not  $S$ ;

20  $R^{27}$  is  $H$ ,  $OH$ , halogen,  $N_3$ ,  $C_1$ - $C_4$  alkyl,  $C_1$ - $C_4$  alkoxy or when,  $R^{26}$  is  $S$ ,  $R^{27}$  is absent;

$R^{28}$  is  $H$ ,  $OH$ , halogen,  $N_3$ ,  $C_1$ - $C_4$  alkyl or  $C_1$ - $C_4$  alkoxy;

R<sup>29</sup> is O, S, CH<sub>2</sub>, CHF or CF<sub>2</sub>;

R<sup>33</sup> is H, OH, TBSO, halogen, cyano, CH<sub>2</sub>N<sub>3</sub>, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, CH<sub>2</sub>OH or azido; and

R<sup>34</sup> is H, CH<sub>2</sub>CN or CF<sub>3</sub>, with the proviso that, for structure XXX,

5 when R<sup>25</sup> is O or CH<sub>2</sub> and R<sup>29</sup> CH<sub>2</sub> or O, R<sup>35</sup> is not H or C<sub>1</sub>-C<sub>6</sub> alkyl; and

provided that when R<sup>25</sup> is CH<sub>2</sub>, R<sup>29</sup> is CH<sub>2</sub>, R<sup>26</sup> is CH, R<sup>27</sup> is H, R<sup>28</sup> is H, and B is adenine, R<sup>35</sup> are not both H or C<sub>3</sub>H<sub>7</sub>; and

provided that when R<sup>25</sup> is O, R<sup>29</sup> is CH<sub>2</sub>, R<sup>26</sup> is S, R<sup>28</sup> is H, and B is cytosine or protected cytosine, R<sup>35</sup> are not both H or ethyl; and

10 provided that when R<sup>25</sup> is CH<sub>2</sub>, R<sup>29</sup> is O, R<sup>26</sup> is CH, R<sup>27</sup> is H, R<sup>28</sup> is H, and B is adenine, guanine, hypoxanthine, cytosine, uracil or thymine, R<sup>35</sup> are not both H or C<sub>3</sub>H<sub>7</sub>; and

provided that when R<sup>25</sup> is O, R<sup>29</sup> is CH<sub>2</sub>, R<sup>26</sup> is CH, R<sup>27</sup> is N<sub>3</sub>, R<sup>28</sup> is H, and B is thymine, R<sup>35</sup> is not H or phenyl; and

15 provided that when R<sup>25</sup> is CH<sub>2</sub>, R<sup>29</sup> is O, R<sup>26</sup> is CH, R<sup>27</sup> is H, R<sup>28</sup> is H, and B is thymine, R<sup>35</sup> is not H or C<sub>1</sub>-C<sub>6</sub> alkyl; and

provided that when R<sup>25</sup> is O, R<sup>29</sup> is CH<sub>2</sub>, R<sup>26</sup> is CH, R<sup>27</sup> is OH, R<sup>28</sup> is H or F, and B is adenine, thymine, guanine, cytosine or protected adenine, protected guanine or protected cytosine, both R<sup>35</sup> are not H, methyl or phenyl;

20 and

provided that when R<sup>25</sup> is O, R<sup>29</sup> is O, R<sup>26</sup> is CH, R<sup>27</sup> is H, OH or C<sub>1</sub>-C<sub>4</sub> alkyl, R<sup>28</sup> is H, OH or C<sub>1</sub>-C<sub>4</sub> alkyl, and B is xanthine, substituted xanthine, guanine, substituted guanine, purine, substituted purine, cytosine, substituted cytosine, thymine, uracil, substituted uracil, adenine or substituted adenine,

25 R<sup>35</sup> is not H or C<sub>1</sub>-C<sub>6</sub> alkyl.

25. The compound of claim 24 wherein R<sup>35</sup> is independently phenyl, benzyl, adamantoyl oxymethyl, pivaloyloxymethyl, 2-methoxyphenyl, 3-methoxyphenyl, 4-methoxyphenyl, 2-fluorophenyl, 3-fluorophenyl, 4-fluorophenyl, 2-ethoxy-5-hydroxyphenyl, 2-ethoxy-4-hydroxyphenyl 3,5-dimethoxyphenyl, 2,4-difluorophenyl, 2-(haloalkyl)-phenyl, 3-(haloalkyl)phenyl, 4-(haloalkyl)-phenyl, 2-cyanophenyl, 3-cyanophenyl, 4-cyanophenyl, 2-ethoxyphenyl, 2-carboethoxyphenyl, 3-carboethoxyphenyl, 4-carboethoxyphenyl, or 2-haloalkylbenzyl, 3-haloalkylbenzyl or 4-haloalkylbenzyl.

26. The compound of claim 25 wherein B<sup>1</sup> is N<sup>4</sup>-benzoylcytosin-1-yl, N<sup>4</sup>-(6-aminohexyl)cytosin-1-yl, N<sup>4</sup>-(10-aminodecyl)cytosin-1-yl, N<sup>4</sup>-(14-aminolauryl)cytosin-1-yl.

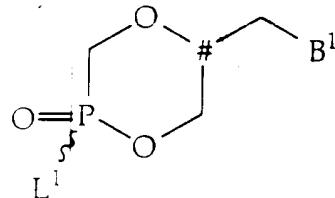
5 27. The compound of claim 1 where L<sup>1</sup> or L<sup>2</sup> is an immunogenic peptide or protein.

10 28. An antibody capable of binding specifically to a compound of claim 27.

15 29. A compound of claim 2 for oral administration of an antivirally-effective dose to a subject.

30. The compound of claim 29 wherein the compound is enriched 15 or resolved at the phosphate atom chiral center.

31. A compound of claim 20 having the structure

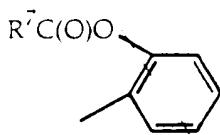


20 for oral administration of antivirally-effective dose to a subject.

32. The compound of claim 31 wherein the compound is enriched or resolved at the phosphate atom chiral center.

25 33. A compound of formula I, wherein the compound is labeled with a detectable moiety selected from the group of an enzyme, radioisotope, stable free radical, fluorophor, and a chemiluminescent group.

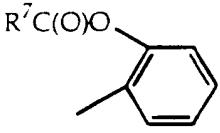
30 34. A compound of the formula (R<sup>31</sup>O)<sub>2</sub>P(O)-CH<sub>2</sub>-OH or (R<sup>31</sup>O)<sub>2</sub>P(OSi(CH<sub>3</sub>)<sub>3</sub>) wherein R<sup>31</sup> is trimethoxybenzyl; triethoxybenzyl; 2-alkyl pyridinyl (C<sub>1-4</sub> alkyl);



wherein R<sup>7</sup> is hydrogen or C<sub>1-4</sub> alkyl; or

C<sub>3</sub>-C<sub>6</sub> aryl substituted by 3, 4 or 5 halogen atoms or 1 or 2 atoms or groups selected from halogen, C<sub>1</sub>-C<sub>12</sub> alkoxy, cyano, nitro, C<sub>1</sub>-C<sub>12</sub> haloalkyl, C<sub>1</sub>-C<sub>12</sub> alkyl or C<sub>2</sub>-12 alkynyl, provided that for compound (R<sup>31</sup>O)<sub>2</sub>P(O)-CH<sub>2</sub>-OH, R<sup>31</sup> is not phenyl.

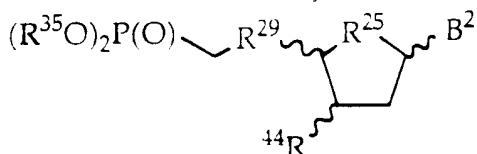
35. A method to synthesize a compound of structure (R<sup>31</sup>O)<sub>2</sub>P(O)-CH<sub>2</sub>-OH comprising silylating a compound of structure (R<sup>31</sup>O)<sub>2</sub>P(O)H with about 1 equivalent of bis(trimethylsilyl)trifluoroacetamide, drying the resulting compound and reacting the resulting compound with paraformaldehyde containing catalytic amounts of a lewis acid, wherein R<sup>31</sup> is trimethoxybenzyl; triethoxybenzyl; 2-alkyl pyridinyl (C<sub>1-4</sub> alkyl);



wherein R<sup>7</sup> is hydrogen or C<sub>1-4</sub> alkyl;

C<sub>3</sub>-C<sub>6</sub> aryl substituted by 3, 4 or 5 halogen atoms or 1 or 2 atoms or groups selected from halogen, C<sub>1</sub>-C<sub>12</sub> alkoxy, cyano, nitro, C<sub>1</sub>-C<sub>12</sub> haloalkyl, C<sub>1</sub>-C<sub>12</sub> alkyl or C<sub>2</sub>-12 alkynyl.

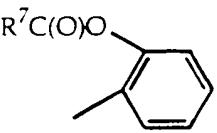
36. A method to synthesize a compound of structure



by reacting a compound of structure



20 with iodine and (R<sup>31</sup>O)<sub>2</sub>P(O)-CH<sub>2</sub>-OH at high temperature, wherein B<sup>2</sup> is a heterocyclic base or a protected heterocyclic base; R<sup>31</sup> is trimethoxybenzyl; triethoxybenzyl; 2-alkyl pyridinyl (C<sub>1-4</sub> alkyl);

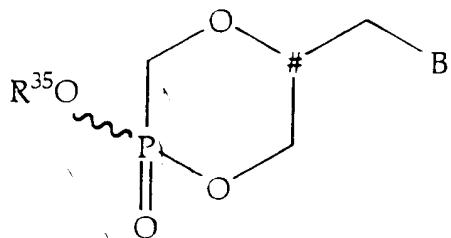


wherein R<sup>7</sup> is hydrogen or C<sub>1-4</sub> alkyl;

$C_3$ - $C_6$  aryl substituted by 3, 4 or 5 halogen atoms or 1 or 2 atoms or groups selected from halogen,  $C_1$ - $C_{12}$  alkoxy, cyano, nitro,  $C_1$ - $C_{12}$  haloalkyl,  $C_1$ - $C_{12}$  alkyl or  $C_2$ - $C_{12}$  alkynyl; and  $R^{44}$  is iodine or fluorine.

5

37. A compound having the formula



and stereoisomers and salts of such compounds wherein

B is a purine or pyrimidine base;

10

$R^{35}$  is R or  $R^{31}$ ;

R is 2-alkoxyphenyl, 3-alkoxyphenyl, 4-alkoxyphenyl ( $C_1$ - $C_{12}$  alkyl), 2-halophenyl, 3-halophenyl, 4-halophenyl, 2,3-dihalophenyl, 2,4-dihalophenyl, 2,5-dihalophenyl, 2,6-dihalophenyl, 3,4-dihalophenyl, 3,5-dihalophenyl, 4-haloalkylphenyl (1-5 halogens,  $C_1$ - $C_{12}$  alkyl), carboalkoxyphenyl ( $C_1$ - $C_4$  alkyl),

15

2-haloalkylbenzyl, 3-haloalkylbenzyl, 4-haloalkylbenzyl (1 to 5 halogen atoms,  $C_1$ - $C_{12}$  alkyl), alkylsalicylphenyl ( $C_1$ - $C_4$  alkyl), alkoxy ethyl ( $C_1$ - $C_6$  alkyl), aryloxy ethyl ( $C_6$ - $C_9$  aryl optionally substituted by OH, NH<sub>2</sub>, halo,  $C_1$ - $C_4$  alkyl or  $C_1$ - $C_4$  alkyl substituted by OH or by 1 to 3 halo atoms), 2-pyrrolyl, 3-pyrrolyl, 2-thienyl, 3-thienyl, 2-imidazolyl, 4-imidazolyl, 2-oxazolyl, 4-oxazolyl, 5-

20

oxazolyl, 3-isoxazolyl, 4-isoxazolyl, 2-thiazolyl, 4-thiazolyl, 5-thiazolyl, 3-isothiazolyl, 4-isothiazolyl, 5-isothiazolyl, 3-pyrazolyl, 4-pyrazolyl, 2-pyridinyl, 3-pyridinyl, 4-pyridinyl, 2-pyrimidinyl, 4-pyrimidinyl, 5-pyrimidinyl, 2-methoxyphenyl, 3-methoxyphenyl, 4-methoxyphenyl, 2-ethoxyphenyl, 3-ethoxyphenyl, 4-ethoxyphenyl, 2-fluorophenyl, 3-fluorophenyl, 4-

25

fluorophenyl, 2,4-difluorophenyl, 2,4-dichlorophenyl, 2-trifluoromethylphenyl, 3-trifluoromethylphenyl, 4-trifluoromethylphenyl, 2-trichloromethylphenyl, 3-trichloromethylphenyl, 4-trichloromethylphenyl, 2-cyanophenyl, 3-cyanophenyl, 4-cyanophenyl, 2-carboethoxyphenyl, 3-carboethoxyphenyl, 4-carboethoxyphenyl (- $C_6$ H<sub>4</sub>-C(O)-OC<sub>2</sub>H<sub>5</sub>), 2,3-

30

dicarboethoxyphenyl, 2,4-dicarboethoxyphenyl, 2,5-dicarboethoxyphenyl, 2,6-dicarboethoxyphenyl, 3,4-dicarboethoxyphenyl, 3,5-dicarboethoxyphenyl, 1-pyridinyl, 2-pyridinyl, 3-pyridinyl, 4-pyridinyl (- $C_5$ H<sub>4</sub>N), 2-nitrophenyl, 3-

nitrophenyl, 4-nitrophenyl, 4-trifluoromethylbenzyl, 2-ethylsalicylphenyl, 3-ethylsalicylphenyl, 4-ethylsalicylphenyl, 2-acetylphenyl, 3-acetylphenyl, 4-acetylphenyl, 1,8-dihydroxy-naphthyl (-O-C<sub>10</sub>H<sub>6</sub>-OH or -O-C<sub>10</sub>H<sub>6</sub>-O-), 2,2'-dihydroxybiphenyl (-O-C<sub>6</sub>H<sub>4</sub>-C<sub>6</sub>H<sub>4</sub>-O-), methoxy ethyl (-CH<sub>2</sub>-CH<sub>2</sub>-O-CH<sub>3</sub>),  
5 phenoxy methyl, phenoxy ethyl, -C<sub>6</sub>H<sub>4</sub>-CH<sub>2</sub>-N(CH<sub>3</sub>)<sub>2</sub> or N-ethylmorpholino -(CH<sub>2</sub>)<sub>2</sub>-N[(CH<sub>2</sub>)<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>]O);

10 R<sup>31</sup> is 2,3-dihydro-6-hydroxyindene, sesamol, catechol monoester, -CH<sub>2</sub>-C(O)-N(R<sup>7</sup>)<sub>2</sub> wherein each R<sup>7</sup> is the same or different, -CH<sub>2</sub>-S(O)(R<sup>7</sup>), -CH<sub>2</sub>-S(O)<sub>2</sub>(R<sup>7</sup>), -O-CH<sub>2</sub>-CH(OC(O)CH<sub>2</sub>R<sup>7</sup>)-CH<sub>2</sub>(OC(O)CH<sub>2</sub>R<sup>7</sup>), cholesteryl, enolpyruvate, glycerol, an  $\alpha$ -D- $\beta$ -diglyceride, trimethoxybenzyl, triethoxybenzyl or 2-alkyl pyridinyl (C<sub>1-4</sub> alkyl);

15 R<sup>7</sup> is H or C<sub>1</sub>-C<sub>4</sub> alkyl; and

the carbon atom designated # has linked substituents that are in the R, S or RS configuration.

15

38. The compound of claim 37 wherein R<sup>35</sup> is R.

10 39. The compound of claim 37 wherein R is 2-alkoxyphenyl, 3-alkoxyphenyl, 4-alkoxyphenyl (C<sub>1</sub>-C<sub>12</sub> alkyl), 2-halophenyl, 3-halophenyl, 4-halophenyl, 2,3-dihalophenyl, 2,4-dihalophenyl, 2,5-dihalophenyl, 2,6-dihalophenyl, 3,4-dihalophenyl, 3,5-dihalophenyl, 4-haloalkylphenyl (1-5 halogens, C<sub>1</sub>-C<sub>12</sub> alkyl), carbalkoxyphenyl (C<sub>1</sub>-C<sub>4</sub> alkyl), 2-haloalkylbenzyl, 3-haloalkylbenzyl, 4-haloalkylbenzyl (1 to 5 halogen atoms, C<sub>1</sub>-C<sub>12</sub> alkyl),  
20 alkylsalicylphenyl (C<sub>1</sub>-C<sub>4</sub> alkyl), alkoxy ethyl (C<sub>1</sub>-C<sub>6</sub> alkyl) or aryloxy ethyl (C<sub>6</sub>-C<sub>9</sub> aryl optionally substituted by OH, NH<sub>2</sub>, halo, C<sub>1</sub>-C<sub>4</sub> alkyl or C<sub>1</sub>-C<sub>4</sub> alkyl substituted by OH or by 1 to 3 halo atoms).

25 40. The compound of claim 39 wherein B is cytosine, 5-fluorocytosine, 5-methylcytosine, adenine, guanine, 2,6-diaminopurine, 2-aminopurine, hypoxanthine or thymine.

30 41. The compound of claim 39 wherein R is alkylsalicylphenyl.

42. The compound of claim 41 wherein B is cytosine.

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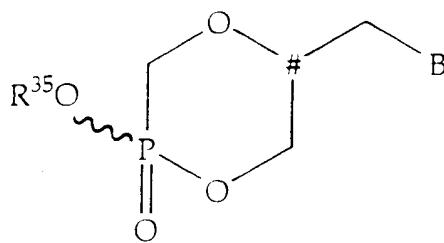
43. The compound of claim 37 wherein R is 2-pyrrolyl, 3-pyrrolyl, 2-thienyl, 3-thienyl, 2-imidazolyl, 4-imidazolyl, 2-oxazolyl, 4-oxazolyl, 5-oxazolyl, 3-isoxazolyl, 4-isoxazolyl, 2-thiazolyl, 4-thiazolyl, 5-thiazolyl, 3-isothiazolyl, 4-isothiazolyl, 5-isothiazolyl, 3-pyrazolyl, 4-pyrazolyl, 2-pyridinyl, 3-pyridinyl, 4-pyridinyl, 2-pyrimidinyl, 4-pyrimidinyl, 5-pyrimidinyl, 2-methoxyphenyl, 3-methoxyphenyl, 4-methoxyphenyl, 2-ethoxyphenyl, 3-ethoxyphenyl, 4-ethoxyphenyl, 2-fluorophenyl, 3-fluorophenyl, 4-fluorophenyl, 2,4-difluorophenyl, 2,4-dichlorophenyl, 2-trifluoromethylphenyl, 3-trifluoromethylphenyl, 4-trifluoromethylphenyl, 2-trichloromethylphenyl, 3-trichloromethylphenyl, 4-trichloromethylphenyl, 2-cyanophenyl, 3-cyanophenyl, 4-cyanophenyl, 2-carboethoxyphenyl, 3-carboethoxyphenyl, 4-carboethoxyphenyl (-C<sub>6</sub>H<sub>4</sub>-C(O)-OC<sub>2</sub>H<sub>5</sub>), 2,3-dicarboethoxyphenyl, 2,4-dicarboethoxyphenyl, 2,5-dicarboethoxyphenyl, 2,6-dicarboethoxyphenyl, 3,4-dicarboethoxyphenyl, 3,5-dicarboethoxyphenyl, 1-pyridinyl, 2-pyridinyl, 3-pyridinyl, 4-pyridinyl (-C<sub>5</sub>H<sub>4</sub>N), 2-nitrophenyl, 3-nitrophenyl, 4-nitrophenyl, 4-trifluoromethylbenzyl, 2-ethylsalicylphenyl, 3-ethylsalicylphenyl, 4-ethylsalicylphenyl, 2-acetylphenyl, 3-acetylphenyl, 4-acetylphenyl, 1,8-dihydroxy-naphthyl (-O-C<sub>10</sub>H<sub>6</sub>-OH or -O-C<sub>10</sub>H<sub>6</sub>-O-), 2,2'-dihydroxybiphenyl (-O-C<sub>6</sub>H<sub>4</sub>-C<sub>6</sub>H<sub>4</sub>-O-), methoxy ethyl (-CH<sub>2</sub>-CH<sub>2</sub>-O-CH<sub>3</sub>), 20 phenoxyethyl, phenoxyethyl, -C<sub>6</sub>H<sub>4</sub>-CH<sub>2</sub>-N(CH<sub>3</sub>)<sub>2</sub> or N-ethylmorpholino (-CH<sub>2</sub>)<sub>2</sub>-N[(CH<sub>2</sub>)<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>]O).

44. The compound of claim 43 wherein B is cytosine, 5-fluorocytosine, 5-methylcytosine, adenine, guanine, 2,6-diaminopurine, 2-aminopurine, hypoxanthine or thymine.

45. The compound of claim 37 wherein B is cytosine, 5-fluorocytosine, 5-methylcytosine, adenine, guanine, 2,6-diaminopurine, 2-aminopurine, hypoxanthine or thymine.

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46. The use a of compound having the formula



and salts of such compounds wherein the carbon atom designated # has linked substituents that are in the R, S or RS configuration, B is cytosine and R<sup>35</sup> is alkylsalicylphenyl (C<sub>1</sub>-C<sub>4</sub> alkyl) in the preparation of a medicament for 5 treating a viral infection by administering an antivirally-effective dose of the compound to an infected subject.

47. The use of the compound in accordance with claim 46 wherein the compound is enriched or resolved at the phosphate atom chiral center.

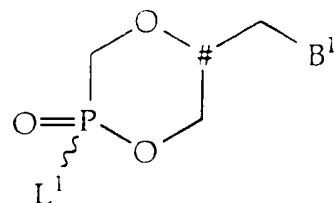
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48. The use of a compound of claim 2 in the preparation of a medicament for treating a viral infection by administering an antivirally-effective dose of the compound to an infected subject.

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49. The use of the compound in accordance with claim 48 wherein the compound is enriched or resolved at the phosphate atom chiral center.

50. The use of a compound of claim 20 having the structure



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in the preparation of a medicament for treating a viral infection by administering an antivirally-effective dose of the compound to an infected subject.

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51. The use of the compound in accordance with claim 50 wherein the compound is enriched or resolved at the phosphate atom chiral center.